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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,671	10/23/2003	Hiroyuki Ishiwata	244288US0DIV	8928
22850	7590	04/11/2006	EXAMINER	
OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			COLEMAN, BRENDA LIBBY	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/690,671	<b>Applicant(s)</b> ISHIWATA ET AL.	
	<b>Examiner</b> Brenda L. Coleman	<b>Art Unit</b> 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-4,6-12 and 14 is/are pending in the application.  
     4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 4,7,9-12 and 14 is/are rejected.
- 7) ☒ Claim(s) 1-3,6 and 8 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/03 &amp; 12/03</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1-4, 6-12 and 14 are pending in the application.

#### ***Election/Restrictions***

1. Applicant's election with traverse of Group I in the reply filed on January 23, 2006 is acknowledged. The traversal is on the ground(s) that in a chemical case, a specified group of materials which do not necessarily belong to the otherwise class can be claimed together employing "Markush language" and that a search of all the claims would not constitute a serious burden on the Office. This is not found persuasive because a diamine of formula (4), a diazepine (where m is 2) and a piperazine (where m is 1) in formula (2), a bispiperazine of formula (3) and an octahydro-pyrazino[1,2-a]pyrazine of formula (5) are clearly structurally dissimilar compound which are classified in various subclasses under classes 546, 544 and 540.

Note MPEP 2173.05(h) "where a Markush expression is applied only to a portion of a chemical compound, the propriety of the grouping is determined by a consideration of the compound as a whole, and does not depend on there being a community of properties in the members of the Markush expression.

Therefore, what should be considered for patentable distinctness is the compound as a whole. If a reference for one would not be a reference for the other, then restriction is considered proper. Community of properties is not enough to keep diamines, diazepines, piperazines and octahydro-pyrazino[1,2-a]pyrazine in the same Markush claim, where the Markush expression is applied only to a portion of a chemical compound. It is the compound as a whole bis(2-aryl-5-pyridyl)diamine, bis(2-aryl-5-

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pyridyl)diazepine, bis(2-aryl-5-pyridyl)piperazine, bis(2-aryl-5-pyridyl) octahydro-pyrazino[1,2-a]pyrazine, etc., that must be considered for patentable distinctness.

Thus, separate searches in the literature would be required. However, should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The degree of burden on the examiner is high. The class/subclass search on the elected invention where the compounds have a bis(2-aryl-5-pyridyl)diamine core would be as follows: class 514, subclasses 332 and 333 and class 546, subclasses 256 and 264 which involved 2371 US patents. The various classes and subclasses mentioned above represent only the degree of burden within the U.S. Patent Classification System, this does not include the search required in the prior art of journal articles and foreign patents.

The requirement is still deemed proper and is therefore made FINAL.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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2. Claims 9-12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of the method claims is not adequately enabled solely based on IgE antibodies provided in the specification. Instant claim language embraces disorders not only for treatment but for prevention which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop allergic immunological disease, asthma, atopic dermatitis, allergic rhinitis, inflammatory bowel disease, contact dermatitis or allergic ophthalmopathy. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Claims 4, 7 and 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claim 4 recites the limitation "said aromatic hydrocarbon group or said aromatic heterocyclic group" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim.

b) Claim 7 recites the limitation "said 1 to 3 substituents" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim.

c) Claims 9-11 are vague and indefinite in that it is not known what is meant by "medicinal composition".

d) Claim 12 is vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being mediated by inhibiting the production of an IgE antibody. It is unclear which diseases are mediated by inhibiting the production of an IgE antibody? Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties in vitro, when administered to a patient with a certain disease, does not produce a favorable response. One cannot conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to

work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration cannot be predicted in advance. Should our drug be given as a bolus iv or in a time release po formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active in vitro, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of which are inhibitors in vitro, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property, which the second drug is capable. It is common for a drug, particularly in area of allergic immunologic, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation

shown to affect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy, which are not themselves effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

### ***Claim Objections***

4. Claim 8 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
5. Claims 1-3 and 6 are objected in that the claims possess non-elected subject matter, i.e. formula (5) in response to the Applicant's election with traverse of Group I in the reply filed on January 23, 2006.



Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Brenda L. Coleman  
Primary Examiner Art Unit 1624  
April 7, 2006